

**Remarks**

The Applicants note the objection to Claims 16, 20 and 22. The Applicants believe that the reference to Claim 22 is a typographical error and that the reference is intended to be Claim 23. Thus, the Response will be treated as directed to Claims 16, 20 and 23.

The Applicants have amended each of Claims 16, 20 and 23 to recite "Met-420 to Glu-511 of metarginin" in accordance with the Examiner's helpful suggestion. Withdrawal of the objection is respectfully requested.

Claim 23 stands rejected under 35 U.S.C. §112 as being indefinite. The Applicants note with appreciation the Examiner's helpful comment with respect to antecedent basis. Claim 23 has accordingly been amended to depend from Claim 24. Claim 24 has been added to provide such antecedent basis. New Claim 24 is the same as Claim 19 except that it depends from Claim 22. Withdrawal of the rejection of Claim 23 is accordingly respectfully requested.

Claims 13 – 23 stand rejected under 35 U.S.C. §112, first paragraph, with respect to enablement. In that regard, the Applicants note with appreciation the Examiner's helpful comment that the Specification is enabled for direct administration of the disintegrin domain, which is Met 420 to Glu 511 of metarginin which corresponds to SEQ ID NO: 1 at a site to be targeted for diminution of the number of intratumoral vessels, for inhibition of growth of melanoma and for inhibition of pulmonary metastases.

The Applicants have amended Claim 13 so that it recites a method of decreasing intratumoral vessels to inhibit growth of melanoma and pulmonary metastases in a mammal in accordance with the Examiner's helpful suggestion. The Applicants accordingly respectfully submit that Claim 13 is in compliance with 35 U.S.C. §112, first paragraph.

Independent Claim 17 has been amended to recite a method of treating melanoma in a mammal comprising decreasing intratumoral vessels to inhibit growth of the melanoma by administering a therapeutically amount of a nucleic acid molecule comprising a polynucleotide sequence of SEQ ID NO: 1. The Applicants respectfully submit that Claim 17 is also in compliance with 35 U.S.C. §112, first paragraph.

Independent Claim 21 has been amended to recite a method of treating pulmonary metastases in a mammal comprising inhibiting the metastases by decreasing intratumoral vessels by administering a therapeutically effective amount of a nucleic acid molecule comprising a polynucleotide sequence of SEQ ID NO: 1. The Applicants respectfully submit that Claim 21 is in compliance with 35 U.S.C. §112, first paragraph.

In light of the above-described amendments to Claims 13, 17 and 21, the Applicants respectfully submit that the subject matter of those claims is now within the subject matter frankly acknowledged by the Examiner as being fully enabled. Withdrawal of the rejection of all of the claims under §112, first paragraph, is respectfully requested.

Claims 13 – 22 stand rejected under 35 U.S.C. §102 as being anticipated by Ruben. The rejection states that Ruben discloses an ADAM protein including metarginin. The rejection also admits that “SEQ ID NO: 1 is not disclosed.” The rejection notes, however, that ADAM molecules are related such that a derivative of SEQ ID NO: 1 is disclosed.

The Applicants respectfully submit that §102 requires that the exact subject matter of a claim be explicitly or implicitly disclosed by the prior art. The Applicants respectfully submit that this is not the case with Ruben inasmuch as the rejection admits that SEQ ID NO: 1 is not disclosed. The three independent claims specifically recite SEQ ID NO: 1. Accordingly, the

Applicants respectfully submit that Ruben inherently does not explicitly or implicitly disclose all of the claimed subject matter.

However, the Applicants also respectfully submit that Ruben fails to disclose treatment of melanoma and pulmonary metastases. As a consequence, the Applicants respectfully submit that Ruben is inapplicable in that regard as well. Withdrawal of the rejection is respectfully requested.

Claims 1, 2 and 4 – 12 stand rejected under 35 U.S.C. §102 as being anticipated by Fanslow. The Applicants respectfully submit that this rejection is moot in view of the earlier cancellation of those claims. Withdrawal of the rejection is respectfully requested.

The Applicants have also cancelled Claim 3, which was previously withdrawn.

In light of the foregoing, the Applicants respectfully submit that the entire Application is now in condition for allowance, which is respectfully requested.

Respectfully submitted,



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